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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/730,214	12/05/2000	Jonathan Miller	13993	9173

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EXAMINER
BORIN, MICHAEL L

ART UNIT	PAPER NUMBER
1631	

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17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/730,214	Miller et al.
Examiner	**Art Unit**
Michael Borin	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 3, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *22-40* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *22-40* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/03/2003 has been entered.

Status of Claims

2. Claims 22-40 are pending.

3. Upon reviewing the application it was deemed necessary to resolve issues addressed in rejections under 35 U.S.C. 112,first and second paragraphs prior to applying appropriate art rejections.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 22-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 22, step three ("normalizing"), and claim 33: According to specification (p. 9), "normalizing" is dividing surface exposure of each amino acid by total surface exposure of the configuration. This is not clear because the preceding method step merely selected the peptide backbone based on set of angles. The backbone is a connection of -NH-(CH2)-CO- moieties, no amino acids are involved in the preceding step, so it is not clear how the surface "of each amino acid" can be estimated. Further, it is not clear what is a "total surface" as related to the backbone.

B. Claim 22, step four ("generating"): The term "random set of sequences" in regard to hydrophobicities, is indefinite because it is not clear what constitutes a "random set"; the term is not defined either in the art or in the specification (p. 9). It is not clear how the set is generated and applied.

Further, The term "uniform weight" is similarly indefinite. It is not clear how "uniform weight" is defined, how it affects generation of the set of sequences of hydrophobicities.

Further, the term "allowed sequences" is not clear. At which point the sequences are identified as "allowed", after the "normalizing" step, or they are sequences from the "random set of sequences of hydrophobicities"?

C. Claim 22, step six ("determining"): the step is vague and indefinite: first it recites one particular configuration ("ground state configuration"), then it addresses plurality of configurations ("desirable configurations"). Further, beginning of the description of the method step suggests that one configuration corresponds to one sequence, but following part of the phrase suggest that many sequences can fall within one configuration. Accordingly, beginning of the claims step addresses ground state of one configuration, while the end recites ground state of "configurations".

D. Claim 22, step seven ("synthesizing"). First, it is not clear what "amino acids" are being addressed: the preceding parts of the claim discuss only a backbone (i.e., a string of -NH-(CH2)-CO- moieties) and do not address any amino acids. Second, for which of the plurality of different "configurations" addressed in the claim, the sequence is synthesized. Finally, as all configurations addressed in the claim differ in their spatial configuration, not their structure, how the preceding steps of the claim relate to the step of "synthesizing"?

E. Claim 27: it is not clear what is the difference of the claimed step from the same step already addressed in claim 22.

F. Claims 28,35: it is not clear what is "non-compact" configurations, which configurations fall within the scope of the term, and how such configurations are eliminated.

G. Claims 29,36,38: the term "sufficiently similar" is indefinite because it is a relative term, but no standard of reference has been provided with which to determine whether a particular configuration is sufficiently similar or not. Accordingly, it is not possible to determine what configurations are embraced within the scope of the claims.

Further, it is not clear from the claim how "clustering configurations" is "followed by their backbones".

Further, it is not clear from the claim which "treating" assumes that all configurations in a cluster as a single configuration.

Further, the term "designability of the cluster" and its involvement in the method step, is not clear.

H. Claims 30,34: which "each configuration" is addressed? Further, how can "designing proteins" start from configurations identified in claims 30,34 if the preceding claims identified a number of steps which has to be executed first before arriving to the step of claims 30,34.

Claim Rejections - 35 USC § 112, first paragraph.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 22-40 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Selection of amino acid components of the protein to be designed is critical or essential to the practice of the invention, but not included in the claims and is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). The only criteria as claimed for generating backbone configuration is selection of dihedral angle pairs. Based only on combination of angles, and backbone configuration without any information on particular amino acid residues and their side chains, an artisan will not be capable of implementing subsequent method steps, such as determining hydrophobicities, evaluating energy, and synthesizing (undefined) protein sequences.

Claim Rejections - 35 U.S.C. § 101/ 112-1

6. Claims 22-40 remain rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a substantial utility

or a well established utility. The rejection is maintained for the following reasons of record:

The invention is drawn to method for designing proteins by a computative method which determines the optimal low energy configuration of a protein. Hence, the asserted utility of the method is making of proteins. However, there is no factual evidence that the proteins produced by such method have a utility (e.g., have any pharmaceutical utility). No specific examples of the claimed design method are present in the specification. Consequently, no protein having any potential utility is disclosed. The specification does not relate to any "real world" substantial utility of the claimed method. Further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use. Note, that prior art acknowledges that design of proteins is largely unsuccessful. See, e.g., Shakhnovitch:

> "Most of the present experimental [protein design] approaches enjoyed only limited success, providing polypeptides that in most cases fold into compact but mostly disordered conformations of molten-globule-like species. It is quite possible that limitations in experimental design result from a relatively low synergism between experiment and theory." p. R45, right column.

The examiner does not find an adequate nexus between the evidence of record and the asserted properties of the claimed subject matter. Identifying use of the claimed polypeptide would require carrying out further research. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real

world" context of use are not substantial utilities. In addition, there is no well established utility known for the method as claimed. Consequently, the claimed subject matter is not supported by substantial or well established utility.

Response to arguments

Applicant argues that the rejection confuses rejection of an invention drawn to a product with the claimed method of designing proteins. Examiner disagrees. Proteins obtained by the method do not have any verifiable "desired" activity. Consequently, investigating whether they have any substantial "desirable" utility will require further research. Accordingly, method of making of products that do not have utility does not have utility itself. As for reference to Fig. 5 that resembles zinc finger protein, the specification is clear on that the structure illustrated on Fig. 5 is not a result of design of desirable protein structure, but rather happened to resemble zinc finger protein configuration. Identifying use of the claimed polypeptide would require carrying out further research. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. The potential specific utilities suggested by applicant are an invitation to do further research to search for a specific and substantial utility for each peptide modeled according to the claimed method.

In regard to "specific" utility of using the method to "design novel small protein structures for use as research tools to address protein folding problem", this utility is not specific as any protein (and/or method of making thereof) can be used to "address protein folding problem". Further, the claims are not drawn to "novel" small protein structures.

In regard to Shakhnovitch reference, Examiner maintains that the reference points at unpredictability of the results of protein design and thus need to further research.

7. Claims 22-40 are also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention.

Applicant argues that specification provides a clear roadmap enabling artisan to perform a method of designing novel proteins. However, rejection addresses "how to use" rather than "how to make" prong of the enablement requirement.

Conclusion.

8. No claims are allowed

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (703) 308-4028. The fax telephone number for this group is (703) 305-3014.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

May 21, 2003

MICHAEL BORIN, PH.D
PRIMARY EXAMINER

mlb